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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,558	03/14/2001	Michael M. Becker	GP068-05.CN3	3920

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EXAMINER	
LACOURCIERE, KAREN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,558	BECKER ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *422-465* is/are pending in the application.

4a) Of the above claim(s) *441-463 and 465* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *422-440 and 464* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-03-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

New claim 465, added with the amendment filed 08-26-2003 is drawn to a method of determining the presence of a nucleic acid analyte in a sample and, therefore, is properly grouped with the method of Group II (claims 441-463), which was not elected. Therefore, new claim 465 is withdrawn.

Applicant's election of 2'-O-methyl as the 2'-O-alkyl species in Paper No. 9, filed 10/1/02, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

This application contains claims 441-463 and 465 drawn to an invention nonelected with traverse in Paper No. 12, filed 01-22-2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 441-463 and 465 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12, filed 1/22/03.

Claim Objections

The objection to claim 422, set forth in the prior Office action, mailed 06-02-2003, is withdrawn in response to Applicant's amendments filed 08-26-2004.

Claim Rejections - 35 USC § 102

The rejection of record of claims 422, 423, 425, 426, 429, 434, 435, 436, 437 and 440 under 35 U.S.C. 102(b) as being anticipated by Azhayeva et al. (*Nucleic Acids Research*, 1995, Vol. 23, No. 21, pp. 4255-4261) , set forth in the prior Office action, mailed 06-02-2003, is withdrawn in response to Applicant's arguments filed 08-26-2004.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 422, 424, 426, 429 and 440 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Lubini et al. (*Current Biology* Vol. 1, No. 1, 1994, pp. 39-45).

Claim 422 is drawn to an oligonucleotide for determining the presence of a nucleic acid analyte in a sample comprising:

a first base region having at least one ribonucleotide modified to include a 2'-O-alkyl

(elected species is a 2'-O-methyl) substitution to the ribofuranosyl moiety; and

a second base region, wherein the first and second base regions hybridize to each other under nucleic acid assay conditions to form a hybrid more stable than a hybrid formed between unmodified forms of the first and second base regions, and wherein the oligonucleotide forms a hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid under nucleic acid assay conditions, such that the nucleic acid analyte can be detected. Claim 440 taught the oligonucleotide of claim 422, wherein the 2'-O-alkyl substitution to the ribofuranyosyl moiety is a 2'-O-methyl substitution.

Lubini et al. taught in Figure 1, page 40, the sequence of a self-complementary 2'-O-methylated RNA-DNA chimera. They further taught that the 2'-O-methyl modification is more stable that the unmodified sequence (abstract). Since the structure of the claimed oligonucleotide was taught by Lubini et al., the claimed functions "for determining the presence of a nucleic acid analyte in a sample" and "such that the

nucleic acid analyte can be detected" would have been an inherent property of the oligonucleotide taught by Lubini et al. Note MPEP 2112.01 that states "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established." Thus, Lubini et al. anticipated all of the claimed limitations.

Claim 424 states the oligonucleotide of claim 422, wherein the first base region includes at least one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

Lubini et al. taught in Figure 1, page 40, that the sequence of the self-complementary oligonucleotide contains some 2'-O-methylated nucleotides (in italics) and the DNA residues are not methylated (in bold).

Claim 426 states the oligonucleotide of claim 422, wherein each nucleotide of the oligonucleotide is a ribonucleotide modified to include a 2'-O-alkyl (2'-O-methyl) substitution to the ribofuranosyl moiety.

The nucleic acid in Figure 1, page 40, shows that only the RNAs (having a ribofuranosyl moiety) are the nucleic acids that are methylated.

Claim 429 states the oligonucleotide of claim 422, wherein the oligonucleotide is between 10 and 100 bases in length. Lubini et al. discloses oligonucleotides within this range.

Claim 434 states the oligonucleotide of claim 422, wherein the oligonucleotide is a hybridization assay probe that forms a detectable hybrid with the nucleic acid analyte.

The oligonucleotide disclosed by Lubini et al. would form a stable hybrid with a suitable analyte.

Response to Arguments

Applicant's arguments filed 08-26-2003 have been fully considered but they are not persuasive. In response to the rejection of record of claims 422, 424, 426, 429 and 440 under 35 U.S.C. 102(b) as being anticipated by Lubini et al. (*Current Biology* Vol. 1, No. 1, 1994, pp. 39-45), Applicant argues that although Lubini et al. discloses oligonucleotides with regions of self-complementary base, Lubini et al. does not demonstrate or suggest that the disclosed RNA-DNA chimera would be capable of self-hybridization under nucleic acid assay conditions. Applicant further argues that the oligonucleotides disclosed by Lubini et al. do not comprise any ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl.

These arguments have been considered but are not persuasive because the oligonucleotides disclosed by Lubini et al. have regions which are fully complementary and, therefore, would inherently be expected to be capable of self-hybridization under nucleic acid assay conditions. Further, the oligonucleotides disclosed by Lubini et al. do comprise ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl at position 5 in the oligonucleotide (see for example, abstract). The claims do not require that the 2'-O-alkyl substitution occur in the self-complementary regions.

Claims 422-440 and 464 are rejected under 35 U.S.C. 102(e) or (a) as being anticipated by Kool et al. (US Patent No 5,514,546).

Kool et al. disclose oligonucleotide hairpins for use in detecting an analyte in a sample, wherein the oligonucleotide comprises 2'-O-alkyl modified bases (see for example, column 13 and column 19, lines 20-38), including 2'-O-methyl. Kool et al. disclose their oligonucleotides wherein the P domain comprises 2'-O-methyl modified bases (wherein the P domain is more than 4 bases long) and wherein the oligonucleotide is a combination of RNA and DNA and, therefore, comprises at least one nucleotide that is not modified by a 2'-O-alkyl in the ribofuranosyl. Kool et al. disclose their oligonucleotides as comprising conjugates and reporter groups, including fluorescent groups (see for example, columns 25-26). Kool et al. disclose their oligonucleotides as capable of use in detecting various analytes, DNA, RNA single and double stranded and as capable of use in amplification assays including PCR and as a capture oligo attached to a solid support (see for example, column 25). It would be expected that the oligonucleotides disclosed by Kool would be capable of detecting any analyte, including rRNA. Therefore, Kool et al. anticipates claims 422-440 and 464.

Claim Rejections - 35 USC § 103

The rejection of record of claims 422, 423, 427, 428, 430, 431, 438 and 439 under 35 U.S.C. 103(a) as being unpatentable over Azhayeva et al. or Lubini et al. in view of Réfrégiers et al., set forth in the prior Office action mailed 06-02-03 is withdrawn in response to Applicant's arguments filed 08-26-2004.

The rejection of record of claims 422, 432 and 433 under 35 U.S.C. 103(a) as being unpatentable over Azhayeva et al. or Lubini et al. 422 and 423, either in view of

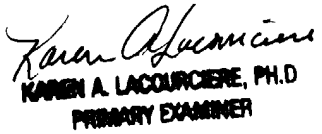
Barry et al. (U.S. Patent 5,574,145) and Roseau et al. (U.S. Patent 5,536,638) is withdrawn in response to Applicant's arguments filed 08-26-04.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Karen A. Lacourciere
August 17, 2004